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10/693,480	10/23/2003	Silviu Itescu	0575/66602-B/JPW/BJA	2572

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COOPER & DUNHAM, LLP
30 Rockefeller Plaza
20th Floor
NEW YORK, NY 10112

EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,480	ITESCU, SILVIU	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,37,43,46,47,49-51 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,37,43,46,47,49-51 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 February 2008 and 23 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/14/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 14 November 2008 has been entered in full. Claims 35, 37, 49, 50 are amended. Claims 1-34, 36, 38-42, 44, 45, 48, and 52-56 are cancelled.

Claims 35, 37, 43, 46, 47, 49, 50, 51, and 57 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The provisional rejection of claims 35-36 and 53-54 on the ground of nonstatutory obviousness-type double patenting over claim 85 of copending Application No. 10/512,518 is *withdrawn* in view of the cancellation of claim 85 in 10/512,518. The remaining claim in the '518 case no longer overlaps with the pending claims in the instant application.

2. The provisional rejection of claims 36, 53-56 on the ground of nonstatutory obviousness-type double patenting over claims 69, 77-78, 82-84 of copending Application No. 11/234,879 are *withdrawn* in view of the cancellation of the these claims (14 November 2008).

Double Patenting

2. Claims 35, 37, 43, 46-47, 49, 50, 51 and 57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 69, 77-78, 82-84 of copending Application No. 11/234,879. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating a disorder comprising administering stromal-derived factor-1. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not

in fact been patented. The basis for this provisional rejection is set forth at page 4 of the previous Office Action (09 May 2008) and pages 6-7 of the Office Action of 08 August 2007.

At page 7 of the Response of 14 November 2008, Applicant requests that if this is the sole remaining ground of rejection, the Examiner withdraw the rejection and allow the claims to issue.

The rejection is maintained and held in abeyance until all other issues are resolved. However, Applicant is encouraged to submit a terminal disclaimer at Applicant's earliest convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 35, 37, 43, 46, 49-51, 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson, BE (US 2002/0094327; priority to 05 November 2000) in view of Hung et al. (US 2003/0171294; priority to 13 August 1999). The basis for this rejection is set forth at pages 4-6 of the previous Office Action (09 May 2008).

At the bottom of page 9 and pages 12-13 of the Response of 14 November 2008, Applicant argues that the combination of prior art does not teach treating a subject suffering a disorder of a heart tissue. Applicant also asserts that the combination does not teach inducing

regeneration of endogenous cardiomyocytes and thereby treating a disorder of a heart tissue involving loss or apoptosis of cardiomyocytes.

(i) Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, Peterson teaches a proposed alternative method for treating organ failure is organ regeneration wherein damaged cells of a failing organ are replaced with new, undamaged cells (page 1, [0004]). Peterson discloses that the invention in the application relates to a method for selectively directing migration of pluripotent stem cells to a target tissue within a subject by modulating the level of SDF-1α protein in the target tissue (page 1, [0006]). Peterson continues to state that by "increasing the number of pluripotent stem cells that traffic to the target tissue, the rate of tissue repair can be increased because there will be a greater number of pluripotent stem cells in the target tissue that can differentiate into cells which can repopulate and partially or wholly restore the normal function of the damaged tissue" (page 1, [0006]). As mentioned in the previous Office Action, Peterson also teaches that the heart is one of the target tissues within a mammalian subject in which SDF-1α is administered (page 8, column 2, [0063]). Thus, in view of Peterson, it is clear that if a mammalian subject has SDF-1 injected into heart tissue, that subject has a damaged heart requiring cell regeneration, meeting the limitations of claim 35.

Additionally, since Peterson et al. teach the administration of SDF-1 to the same subject population and to the same tissue as recited in the claims, the regeneration of endogenous cardiomyocytes must have been inherently occurring in the prior art. The disclosure of Peterson fully meets the terms of the claimed method because SDF-1α inherently possesses cardiomyocyte regeneration activity, absent evidence to the contrary (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). A compound and all of its properties are inseparable;

they are one and the same thing and simply stating a new property of SDF-1α does not render the claimed method of the instant application free of the art (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971); *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)).

(ii) Applicant submits that Peterson is directed to a method of directing stem cell to selected tissues by administering SDF-1. Applicant argues that this is a fundamentally different concept to that of administering SDF-1 to a selected tissue in order to protect or enhance proliferation of cells endogenous to that tissue. Applicant adds that Hung et al. does not cure this deficiency. Applicant's arguments have been fully considered but are not found to be persuasive. As mentioned above, the disclosure of Peterson fully meets the terms of the claimed method because SDF-1α inherently possesses cardiomyocyte regeneration activity, absent evidence to the contrary (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). A compound and all of its properties are inseparable; they are one and the same thing and simply stating a new property of SDF-1α does not render the claimed method of the instant application free of the art (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971); *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)). Furthermore, according to Peterson, "increasing the number of pluripotent stem cells that traffic to the target tissue, the rate of tissue repair can be increased because there will be a greater number of pluripotent stem cells in the target tissue that can differentiate into cells which can repopulate and partially or wholly restore the normal function of the damaged tissue" (page 1, [0006]).

Hence, one skilled in the art would recognize that pluripotent stem cells that traffic to the heart tissue (due to administration of SDF-1 α) will differentiate into cells, such as cardiomyocytes.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., administration of SDF-1 to a selected tissue in order to protect or enhance proliferation of cells endogenous to that tissue) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

(iii) At the bottom of page 10, Applicant argues that there is nothing in Hung et al. to suggest administration of SDF-1 to the heart. Applicant submits that Hung et al. only describes the administration of an angiogenic factor to the myocardium in order to induce angiogenesis in the heart. Applicant states that this concept is not related to the method described in Peterson, which concerns mobilization of stem cells to specific tissue sites. Applicant's arguments have been fully considered but are not found to be persuasive. Peterson teaches that SDF-1α can be introduced into target tissues, such as the heart, in a mammalian subject (page 8, column 2, [0063]). Hung et al. simply discloses the successful intramyocardial and intracoronary administration of therapeutic proteins, such as FGF, to subjects. Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of administering of SDF-1α to heart tissue as taught by Peterson by utilizing intramyocardial or intracoronary administration as taught by Hung et al. The person of ordinary skill in the art would have been motivated to make that modification in order to localize cell

migration/differentiation and tissue repair (see for example, Hung et al. page 1, [0007]). The person of ordinary skill in the art reasonably would have expected success because similar proteins and agents were already being intramyocardially and intracoronarily administered to the heart at the time the invention was made (see Hung et al.). Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

4. Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson, BE (US 2002/0094327; priority to 05 November 2000) and Hung et al. (US 2003/0171294; priority to 13 August 1999) as applied to claims 35-37, 43, 46, 49-51, 53-57 above, and further in view of Rempel et al. (Clin Can Res 6: 102-111, 2000). The basis for this rejection is set forth at pages 6-7 of the previous Office Action (09 May 2008).

(i) At page 12 of the Response, Applicant argues that Rempel et al. teach the use of SDF-1 to treat subjects with glioblastoma tumors rather than to treat subjects with diseases of the heart. Applicant states that it would not have been obvious to the person of ordinary skill in the art to modify the method of intramyocardially or intracoronarily administering SDF-1α to heart tissue as disclosed in Peterson and Hung et al. by substituting SDF-1α with SDF-1β. Applicant asserts that in the absence of applicant's discovery, there would be no motivation to use SDF-1β in the method disclosed by Peterson. Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in the previous Office Action, Rempel et al. teaches that the SDF-1 gene encodes two isoforms, SDF-1α and SDF-1β, that arise from alternative splicing (page 102, column 2, last paragraph). Rempel et al. also disclose that these isoforms differ only

in that SDF-1β contains four additional 3' amino acids (page 102, column 2, last paragraph). Both isoforms interact with the same seven-transmembrane G protein-coupled receptor, CXCR4 (page 103, column 1, 1st full paragraph). Hence, SDF-1α and SDF-1β have the same function. Rempel et al. also disclose SDF1-deficient mice exhibit hematopoietic, cardiac, and cerebellar defects (page 103, column 1, bottom of 1st full paragraph). Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of intramyocardially or intracoronarily administering SDF-1α to heart tissue as taught by Peterson and Hung et al. by substituting SDF-1α with SDF-1β as taught by Rempel et al. Since Rempel et al. teach that SDF-1α and SDF-1β are isoforms encoded from the SDF-1 gene and that SDF-1β only contains four additional amino acids as compared to SDF-1α, one skilled in the art would have been motivated to substitute the utilization of SDF-1α for the SDF-1β to achieve the predictable result of treating a subject suffering from damaged heart tissue.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
27 January 2009

/Bridget E Bunner/
Primary Examiner, Art Unit 1647